CLAIMS

We claim:

1. A crystallizable composition comprising

a) a purified enzyme selected from unphosphorylated JNK1, unphosphorylated JNK2, unphosphorylated JNK3, or an unphosphorylated isoform of said enzyme, wherein said enzyme contains a C-terminal deletion of about 20 amino acids and, if said enzyme is unphosphorylated JNK3, said enzyme additionally contains an N-terminal deletion of about 40 amino acids;

b) a non-hydrolyzable ATP analog or a suicidal substrate;

c) magnesium ions;

d) between about 10 to 30% v/v polyethylene glycol monomethyl ether;

e) between about 5 to 20% v/v ethylene glycol;

f) a reducing agent at a final concentration of between about 5 to 50 mM; and

g) a buffer that maintains pH at between about 7.0 and 7.5.

2. The crystallizable composition according to claim 1, wherein said unphosphorylated JNK3 enzyme is JNK3α1.

3. The composition according to claims 1 or 2, wherein said non-hydrolyzable ATP analog is AMP-PNP.

4. A crystallized complex capable of being resolved at 2.3 Å resolution comprising:

a) a purified enzyme selected from unphosphorylated JNK1, unphosphorylated JNK2, unphosphorylated JNK3, or an unphosphorylated isoform of said enzyme, wherein said enzyme contains a C-terminal deletion of about 20 amino acids and, if said enzyme is

unphosphorylated JNK3, said enzyme additionally contains an N-terminal deletion of about 40 amino acids;

b) a non-hydrolyzable ATP analog or a suicidal substrate; and

c) magnesium ions.

5. The crystallized complex according to claim 4, wherein said unphosphorylated JNK3 enzyme is JNK3α1.

6. The crystallized complex according to claim 4, wherein said non-hydrolyzable ATP analog is AMP-PNP.

7. A method of obtaining a crystal comprising a purified enzyme selected from unphosphorylated JNK1, unphosphorylated JNK2, unphosphorylated JNK3, or an unphosphorylated isoform of said enzyme, said crystal being capable of being resolved at 2.3 Å resolution, comprising the step of subjecting a composition according to claims 1 or 2 to conditions which promote crystallization.

8. A computer for producing a three-dimensional representation of:

a) a molecule or molecular complex, wherein said molecule or molecular complex comprises a binding pocket defined by structure coordinates of JNK3 amino acids Ile70, Gly71, Ser72, Gly73, Ala74, Gln75, Gly76, Val78, Ala91, Lys93, Glu111, Ile124, Met146, Glu147, Leu148, Met149, Asp150, Ala151, Asn152, Gln155, Lys191, Ser193, Asn194, Val196 and Leu206, according to Figure 1; or

b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the

backbone atoms of said amino acids of not more than 1.5 Å,

wherein said computer comprises:

(i) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said data comprises the structure coordinates of JNK3 amino acids Ile70, Gly71, Ser72, Gly73, Ala74, Gln75, Gly76, Val78, Ala91, Lys93, Glu111, Ile124, Met146, Glu147, Leu148, Met149, Asp150, Ala151, Asn152, Gln155, Lys191, Ser193, Asn194, Val196 and Leu206, according to Figure 1;

(ii) a working memory for storing instructions for processing said machine-readable data;

(iii) a central-processing unit coupled to said working memory and to said machine-readable data storage medium for processing said machine readable data into said three-dimensional representation; and

(iv) a display coupled to said central-processing unit for displaying said three-dimensional representation.

9. The computer according to claim 8, wherein said computer produces a three-dimensional representation of:

a) a molecule or molecular complex comprising a binding pocket defined by the structure coordinates of JNK3 amino acids Ile70, Gly71, Ser72, Gly73, Ala74, Gln75, Gly76, Ile77, Val78, Cys79, Ala80, Val90, Ala91, Ile92, Lys93, Lys94, Leu95, His104, Arg107, Glu111, Ile124, Ser125, Leu144, Val145, Met146, Glu147, Leu148, Met149, Asp150, Ala151, Asn152, Leu153, Cys154, Gln155, Asp189, Lys191, Pro192, Ser193, Asn194, Ile195, Val196 Val197, Lys204, Leu206 and Asp207, according to Figure 1; or

b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the

backbone atoms of said amino acids of not more than 1.5 Å; and

wherein said machine readable data comprises the structure coordinates of JNK3 amino acids Ile70, Gly71, Ser72, Gly73, Ala74, Gln75, Gly76, Ile77, Val78, Cys79, Ala80, Val90, Ala91, Ile92, Lys93, Lys94, Leu95, His104, Arg107, Glu111, Ile124, Ser125, Leu144, Val145, Met146, Glu147, Leu148, Met149, Asp150, Ala151, Asn152, Leu153, Cys154, Gln155, Asp189, Lys191, Pro192, Ser193, Asn194, Ile195, Val196 Val197, Lys204, Leu206 and Asp207, according to Figure 1.

10. The computer according to claims 8 or 9, wherein said computer produces a three-dimensional representation of:

a) a molecule or molecular complex defined by structure coordinates of JNK3 amino acids set forth in Figure 1; or

b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 Å; and

wherein said machine readable data contains the coordinates of JNK3 complex set forth in Figure 1.

SUB A1

11. A computer for determining at least a portion of the structure coordinates corresponding to X-ray diffraction data obtained from a molecule or molecular complex, wherein said computer comprises:

a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said data comprises at least a portion of the structural coordinates of the JNK3 complex according to Figure 1;

b) a machine-r

comprising a data storage materi storage medium

reable data, wherein said data com with machin-

diffraction data obtained from said mo molecular

complex;

c) a working memory for stori uctions

for processing said machine-readable data of (a)

d) a central-processing unit coupl (b);

working memory and to said machine-readable data store said

medium of (a) and (b) for performing a Fourier transform

of the machine readable data of (a) and for processing

said machine readable data of (b) into structure

coordinates; and

e) a display coupled to said central-

processing unit for displaying said structure coordinates

of said molecule or molecular complex.

12. A method for evaluating the potential of a chemical entity to associate with:

a) a molecule or molecular complex comprising a binding pocket defined by structure coordinates of JNK3 amino acids Ile70, Gly71, Ser72, Gly73, Ala74, Gln75, Gly76, Val78, Ala91, Lys93, Glu111, Ile124, Met146, Glu147, Leu148, Met149, Asp150, Ala151, Asn152, Gln155, Lys191, Ser193, Asn194, Val196 and Leu206 according to Figure 1; or

b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 A,

said method comprising the steps of:

(i) employing computational means to perform a fitting operation between the chemical entity and a binding pocket of the molecule or molecular complex; and

(ii) analyzing the results of said fitting operation to quantify the association between the chemical entity and the binding pocket; and

(iii) outputting said quantified association to a suitable output hardware.

13. The method according to claim 12, wherein said method evaluates the potential of chemical entity to associate with:

a) a molecular or molecular complex comprising a binding pocket defined by the structural coordinates of JNK3 amino acids Ile70, Gly71, Ser72, Gly73, Ala74, Gln75, Gly76, Ile77, Val78, Cys79, Ala80, Val90, Ala91, Ile92, Lys93, Lys94, Leu95, His104, Arg107, Glu111, Ile124, Ser125, Leu144, Val145, Met146, Glu147, Leu148, Met149, Asp150, Ala151, Asn152, Leu153, Cys154, Gln155, Asp189, Lys191, Pro192, Ser193, Asn194, Ile195, Val196 Val197, Lys204, Leu206 and Asp207, according to Figure 1;or

b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 A.

14. The method according to claims 12 or 13, wherein said method evaluates the potential of a chemical entity to associate with a molecule or molecular complex:

a) defined by the set of structure coordinates for JNK3 amino acids, as set forth in Figure 1; or

b) a homologue of said molecule or molecular complex having a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 Å.

15. A method of obtaining structural information about a molecule or a molecular complex whose structure is unknown, comprising the steps of:

a) crystallizing said molecule or molecular complex of unknown structure;

b) generating an X-ray diffraction pattern from said crystallized molecule or molecular complex; and

c) applying at least a portion of the structure coordinates set forth in Figure 1 to the X-ray diffraction data to generate a three-dimensional electron density map of at least a portion of the molecule or molecular complex whose structure is unknown.

16. A method for identifying a potential agonist or antagonist of a molecule comprising a JNK3-like binding pocket, comprising the steps of:

a) using the atomic coordinates of Ile70, Gly71, Ser72, Gly73, Ala74, Gln75, Gly76, Val78, Ala91, Lys93, Glu111, Ile124, Met146, Glu147, Leu148, Met149, Asp150, Ala151, Asn152, Gln155, Lys191, Ser193, Asn194, Val196 and Leu206 according to Figure 1 ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 Å, to generate a three-dimensional structure of molecule comprising a JNK3-like binding pocket;

b) employing said three-dimensional structure to design or select said potential agonist or antagonist;

c) synthesizing said agonist or antagonist; and

d) contacting said agonist or antagonist with said molecule to determine the ability of said potential agonist or antagonist to interact with said molecule.

17. The method according to claim 16, wherein the atomic coordinates of Ile70, Gly71, Ser72, Gly73, Ala74, Gln75, Gly76, Ile77, Val78, Cys79, Ala80, Val90, Ala91, Ile92, Lys93, Lys94, Leu95, His104, Arg107,

Glu111, Ile124, Ser125, Leu144, Val145, Met146, Glu147, Leu148, Met149, Asp150, Ala151, Asn152, Leu153, Cys154, Gln155, Asp189, Lys191, Pro192, Ser193, Asn194, Ile195, Val196 Val197, Lys204, Leu206 and Asp207 according to Figure 1 ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 Å, are used to generate said three-dimensional structure of the molecule comprising a JNK3-like binding pocket.

18. The method according to claims 16 or 17, wherein the atomic coordinates of the amino acids of JNK3 according to Figure 1 ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 Å, are used to generate a three-dimensional structure of molecule comprising a JNK3-like binding pocket.